per kg. of body weight into hypersensitive dogs show an increased toxicity similar to that observed with normal dogs. At the end of 6 hours the toxicity is approximately that of the control horse serum dose. By the end of 10 hours the toxicity is reduced to about a quarter of the control dose. By the 15th hour the circulating blood usually becomes completely nontoxic.

Precipitin titrations show no reduction in the amount of circulating horse protein in the injected hypersensitive dog at this time.

In so far as a complete anaphylactic detoxication of horse proteins takes place by the end of 4 days in normal dogs, there is no reason to believe that the hypertrophy of this detoxicating function observed in hypersensitive dogs is necessarily due to specific antibodies.

This is a preliminary report.

[1] Manwaring, W. H., Marino, H. D., McClure, T. C., and Boone, T. H., PROC. SOC. EXP. BIOL. AND MED., 1927, xxiv, 553.

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Toxic Substances in Friedlander's Bacillus Cultures.

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Two substances, toxic for rabbits, were produced in cultures of a strain of Friedlander's bacillus, originally isolated from an epidemic of pneumonia among guinea pigs.

The organism is highly pathogenic for guinea pigs and rabbits by any route of injection. Mice are also readily infected by intraperitoneal injection; a dilution of 1 :10 billion of a 24-hour old broth culture (5-20 bacteria) produces the characteristic sticky mucoid exudate. Culturally, the organism forms acid but no gas in glucose, lactose, saccharose, maltose, mannite, and salicin, but not dulcite. It also reduces nitrates to nitrites, and gives a negative methyl red and Voges-Proskauer reaction.

Toxic Substance A. Procedure: The organism was grown in Huntoon's hormone broth containing 2 per cent peptone, in shallow layers in pint bottles, 20 cc. to a bottle giving a depth of 3/8 inch. The bottles were shaken once a day. The cultures were finally filtered through Berkefeld (N) candles. The pH and M.L.D. of the toxin for rabbits were determined at regular intervals.

* Edythe Claypole Memorial Fellowship.

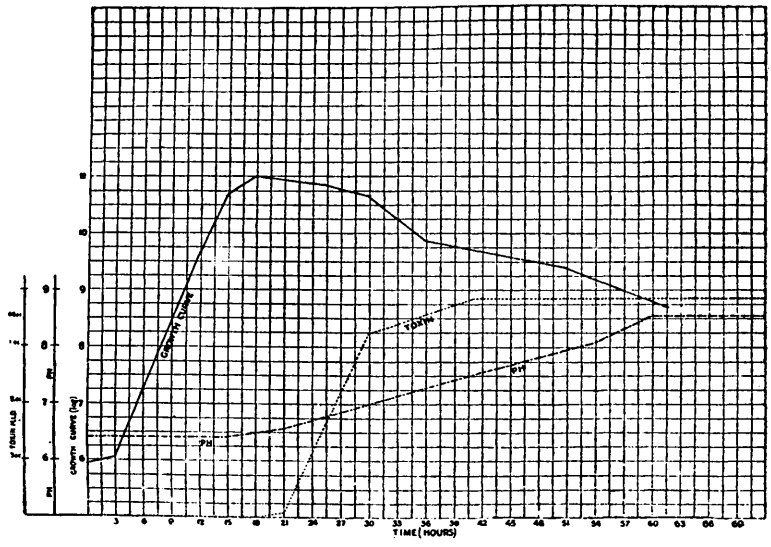

CHART 1.
Relationship between toxin production, growth curve, and pH.

As shown in Chart 1, the toxicity of the broth filtrate begins to rise after the growth curve has exhibited a tendency to descend, and after the pH has risen above 7.0. In several experiments, the peak of the toxin curve was reached when the pH was between 8.0 and 8.6, then the toxicity remained constant for several days.

Rabbits inoculated intravenously appeared sick within 2 to 6 hours. The animals were weak and depressed; the breathing was labored and rapid, and there was profuse watering of the eyes. The dyspnea increased until the respiration showed marked wheezing and evidence of much moisture in the lungs and trachea. As a rule the animals died in from 5 to 24 hours.

On postmortem examination the lungs were large, moist, dark red and firm. The cut surface was very wet, and edematous fluid could be expressed from the alveoli and bronchi. Histologically, the alveoli and bronchi were filled by a finely granular material which in some places compressed the bronchi to a narrow slit. There was marked engorgement of the blood vessels, with small hemorrhages into the interalveolar regions. The trachea was reddish black in color, the vessels being markedly injected; the thymus showed extensive extravascular hemorrhages. The heart was dilated, the right ventricle more than the left. The other organs presented the appearance of cloudy swelling and congestion.

The blood of the rabbits, receiving gradually increasing doses of the toxin, transferred no passive immunity, but the animals ac-

quired a marked tolerance, and withstood in some of the tests as much as 10 M.L.D of the toxin.

The toxin frequently resisted boiling for 5 minutes.

Toxic Substance B. The organisms were grown semi-anaerobically in test tubes for 24 hours, then centrifugalized for one hour at high speed and the supernatant fluid injected intravenously. Three to five cc. of the supernatant fluid killed rabbits in from 6 to 24 hours. Passage through a Berkefeld filter removed the toxic properties. Intravenous inoculation into rabbits was followed by an incubation period of from 1 to 2 hours. The animals exhibited weakness, muscular relaxation, diarrhea, slight watering of the eyes, and died suddenly in convulsions, usually within 7 hours. This toxic substance had an aggressine-like action. It was not antigenic. Rabbits, inoculated with gradually increasing doses, lost weight; they failed to develop any degree of resistance. Autopsy findings, for the most part, showed merely engorgement of the intestinal vessels. This substance is probably identical with the toxic products in young cultures, reported by Zinsser and collaborators[1] for the streptococcus, dysentery and typhoid bacilli, and other organisms.

Summary. Cultures of a strain of Friedlander's bacillus were found to yield two toxic substances; one, produced in aerobic cultures, which has a selective affinity for the lungs causing small pulmonary hemorrhages and an intense edema; the other, produced under semi-anaerobic conditions of growth, is probably a non-specific toxic product possessing an aggressine-like action.

[1] Zinsser, H., Parker, J. T., and Kuttner, A., PROC. SOC. EXP. BIOL. AND MED., 1920, xviii, 49.

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Pharmacology of Veratrum Californicum.

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Veratrum Californicum Durand has not been previously studied pharmacologically. Botanically, it is closely related to *Veratrum viride* and *Veratrum album,* although certain differences for identification purposes have been described by Viehover, Keenan and Clevenger, and Viehover and Clevenger.[1] The active constituents